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Committee on Energy and Commerce
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JOHN D. DINGELL, MICHIGAN
CHAIRMAN

June 6, 2007

MEMORANDUM

TO: Members, Subcommittee on Health

FROM: Frank Pallone, Jr., Chairman
Subcommittee on Health

SUBJECT: Discussion Drafts of Legislation on PDUFA, MDUFMA, Drug Safety, Pediatric Rule, Pediatric Incentive, and Pediatric Devices

Attached are discussion drafts of legislation to reauthorize four Acts pertaining to prescription pharmaceuticals and medical devices. These include:

- Prescription Drug User Fee Act (PDUFA)
- Medical Device User Fee and Modernization Act (MDUFMA)
- Pediatric Research Equity Act (PREA)
- Best Pharmaceuticals for Children Act (BPCA)

Also attached are discussion drafts on drug safety and pediatric medical devices. The drug safety legislation has been divided into four distinct committee prints:

- Risk Evaluation and Mitigation Strategies
- Clinical Trial Registry Database and Clinical Trial Results Database
- Food and Drug Administration Advisory Panels Conflicts of Interest
- The Reagan-Udall Institute for Applied Biomedical Research

The Subcommittee on Health has held hearings this year on each of the programs and issues contained in these legislative proposals. I welcome comments and suggestions from all members on the attached language. I anticipate holding a Subcommittee markup on these discussion drafts Thursday, June 14, 2007, following the legislative hearing announced for next Tuesday, June 12, 2007. This memo will review the background and need for legislation.

REAUTHORIZATIONS

Prescription Drug and User Fee Act (PDUFA) IV

Originally enacted in 1992, the Prescription Drug User Fee Act provides an additional revenue source for the Food and Drug Administration (FDA) to expedite review of drug and biologic product approval applications and subsequent drug safety monitoring. PDUFA was reauthorized in 1997 and 2002. PDUFA expires on September 30, 2007, prompting Congressional action for its third reauthorization. PDUFA fees represent more than half of FDA's resources for review of new drugs and biologics. Accordingly, a failure to reauthorize PDUFA in a timely manner could result in a severe disruption in FDA's drug and biologics programs. PDUFA fees are collected on facilities that manufacture drugs and biologics, products already on the market, and on applications for product approval, and applications, known as supplements, for changes to already marketed products. Approximately one-third of the revenues generated by PDUFA come from each source: facilities, products, and applications.

The discussion draft would reauthorize PDUFA through FY2012. Proposed changes to the prescription drug user fee program fall into three major categories: (1) enhancements to ensure sound financial footing for the human drug review program; (2) enhancements for pre-market review of human drug applications; and (3) enhancements to modernize and transform the post-market safety system. The PDUFA discussion draft includes an increase in the total annual user fees collected to $392.8 million for FY2008, an $87.4 million increase over the current base. The discussion draft provides for increases in PDUFA fees to take into account inflation and increased resources needed to conduct certain activities, known as a workload adjustment.

The Administration has indicated that, of the $87.4 million increase in the total annual user fees collected, $49.4 million will be used to adjust for inflation and increases in salaries and benefits, to cover a share of increased rents and agency moves, and to cover significant increases in FDA's drug review workload that were incurred, but not compensated, for under PDUFA III.

An additional $8.6 million will enhance the process for pre-market review of human drug applications. Specifically, these funds will be used to expand FDA's implementation of Good Review Management Principles for reviewers and guidelines for industry. A substantial investment will also be made to improve the information technology infrastructure for human drug review efficiency.

Activities that take place after FDA approves a product are referred to as "post-market." Originally, PDUFA fees were applied solely to pre-market review activities. The 2002 reauthorization changed this to allow, for the first time, allocation of user fees for some post-market activities. The discussion draft expands the amount and scope of fees devoted to post-market safety with an additional $225 million in user fees above the Administration's proposal over 5 years. The draft eliminates the current three-year limitation on the use of fees for post-market surveillance.

The discussion draft would establish a new program to assess, collect, and use fees for the voluntary review of prescription drug direct-to-consumer (DTC) television advertisements. A one-time fee will be assessed at the beginning of the program, or when a company first elects to participate, in addition to a fee that will be charged for each advisory review requested. This new fee is expected to generate over $6 million per year. This would support a significant increase in the resources currently allocated to review of DTC advertising.

The discussion draft provides an establishment fee reduction for manufacturers that produce compounded positron emission tomography (PET) drugs. PET drugs are used in the treatment and diagnosis of conditions such as cancer, Alzheimer's disease, and heart disease, and the potential application of significant establishment fees can place an unreasonable economic burden on the facilities that manufacture them. The manufacturer would be subject to one-sixth of the annual establishment fee. In certain instances, the Secretary would be granted the authority to waive the establishment fee.

Finally, in anticipation of PDUFA V, the discussion draft would require greater transparency in negotiations between the drug companies and biotechnology firms that pay fees to FDA by allowing other stakeholders such as consumer and patient advocates to participate in the negotiations for PDUFA V.

Medical Device User Fee and Modernization Act

Originally enacted in 2002, the Medical Device User Fee and Modernization Act (MDUFMA), provides an additional revenue source for FDA to review medical devices. FDA's authority to collect medical device user fees expires on October 1, 2007, prompting Congressional action for reauthorization. Without this reauthorization, FDA could lose a number of employees who currently review medical device applications.

The MDUFMA discussion draft would reauthorize medical device user fees through FY 2012. Enhancements to the medical device program fall into two major categories: (1) enhancements to ensure sound financial footing for the device review program; and (2) enhancements to the process for pre-market review of device applications.

Under the discussion draft, companies would pay 31 percent more in fees in 2008 and 8.5 percent more each subsequent year through 2012. This will ensure fee increases from year to year over the next five years to cover anticipated costs related to rent, security, and statutorily mandated payroll and benefit increases. The $287 million in industry fees collected during the five-year reauthorization period would account for about 23 percent of the more than $1.2 billion FDA estimates it needs to adequately review medical devices.

In an effort to add stability to this fee program, the discussion draft includes two new types of fees, which would generate about 50 percent of the total fee revenue. The new fees are an annual establishment registration fee and an annual fee for filing periodic reports.

One effect of the new fees is to reduce application fees across the board. The fees paid by device manufacturers that meet the definition of "small" would also be reduced. Small business provisions would also be expanded to provide a way for foreign firms that do not file tax returns with the United States Internal Revenue Service to qualify for small business rates.

Under current law, fees can be used to fund the evaluation of post-market studies that are required as a condition of approval. The discussion draft would also authorize appropriations for additional post-market safety activities. Additionally, it would require that the Secretary of Health and Human Services report to Congress no later than one year after enactment of this Act what post-market activities are being funded through user fees, with subsequent reports in each following year through FY2012. The MDUFMA discussion draft would keep in place current requirements for third-party inspections, such as a requirement that device manufacturers petition FDA for clearance to use a third party and limits manufacturers to two consecutive third-party inspections, after which FDA must conduct the next inspection, unless the manufacturer petitions and receives a waiver.

Finally, in anticipation of MDUFMA III, the discussion draft would require greater transparency in negotiations between the device companies that pay fees to FDA by allowing other stakeholders such as consumer and/or patient advocates to participate in the negotiations for MDUFMA III.

Best Pharmaceuticals for Children Act

The Best Pharmaceuticals for Children Act (BPCA) provides FDA with the authority to grant marketing exclusivity to a manufacturer of a drug in return for FDA-requested pediatric use studies and reports. The discussion draft proposes a new exclusivity model to range between a floor of three months and a ceiling of six months. FDA would be required to establish a rule in which it would outline the standards used to determine the amount of exclusivity a manufacturer would receive in exchange for conducting a requested pediatric study. In establishing such a rule, FDA would consider, in part, the combined annual gross sales for the drug in which a study has been requested relative to the research and development expenses incurred for conducting the pediatric study. BPCA also includes provisions to encourage research for products that are off-patent or for products whose manufacturer declines to conduct FDA-related studies.

The BPCA discussion draft would make a variety of modifications to current law. The discussion draft would increase to 180 days, the time limit that the Secretary has for deciding whether to grant exclusivity. Labeling requirements would be strengthened to ensure that labels reflect study results in a timely and consistent fashion. A toll-free number for reporting adverse events would also be added to product labels.

Pediatric Research Equity Act

The Pediatric Research Equity Act requires a manufacturer of a drug or biologic who submits an application to market a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration to also submit a pediatric assessment. Under the discussion draft, the provision in current law that would sunset the program would be eliminated. Thus, the Secretary would have permanent authority to require pediatric tests in appropriate circumstances. Provisions of current law that allow a deferral of pediatric tests for new products would be strengthened in substance and shortened in duration. The standard for requiring tests for already marketed drugs would also be strengthened. Requirements with respect to labeling drugs would be strengthened to ensure that they reflect in a timely way the results of studies.

ADDITIONAL LEGISLATION

Drug Safety: Risk Evaluation and Mitigation Strategy (REMS)

The drug safety discussion draft would strengthen FDA's post-market drug safety authority, provide greater FDA transparency, and establish mandatory clinical trial registry and results databases. Specifically, the drug safety discussion draft would provide FDA with the authority to require labeling changes under appropriate circumstances. The discussion draft would provide for an increased level of civil monetary penalties for violations of the Federal Food Drug and Cosmetic Act. The Secretary would be granted the authority to place a temporary waiting period of up to three years on direct-to-consumer advertisements for new drugs in circumstances deemed necessary by the Secretary to protect public health. This authority would be applied on a case-by-case basis.

The discussion draft also provides FDA with enhanced tools to ensure post-market drug safety through a "Risk Evaluation and Mitigation Strategy" process. All applications would be required to include a REMS. The Secretary would have the authority to waive this requirement in certain circumstances. The discussion draft adopts the Institute of Medicine's recommendation that FDA place a symbol on the packaging of a product to let consumers know that the drug is new to the marketplace. In addition, FDA is required to report to Congress on its efforts to integrate the expertise of the Office of Surveillance and Epidemiology (formerly known as the Office of Drug Safety) into the Agency's approval, labeling, and post-approval safety decisions.

The discussion draft requires FDA to review data on the use of drug products after they have been on the market for seven years. It also directs the Secretary to establish an active post-market drug surveillance infrastructure.

Drug Safety: Clinical Trial Registry Database and Clinical Trial Results Database

The discussion draft would establish two separate databases: one for a clinical trial registry and the other for clinical trial results. All clinical trials that are conducted to test the safety and efficacy of both drugs and devices would be subject to the database reporting requirements. The databases would apply to both private and publicly-funded clinical trials. The draft would require that the clinical trials registry and clinical trial results database be made publicly available through the Internet. In addition, the discussion draft requires that the requisite clinical trial information for the results database be made available to the public within a specified period.

The discussion draft also provides civil monetary penalties (CMPs) for noncompliance with the 30-day disclosure period. The discussion draft makes retroactivity of the database voluntary.

Drug Safety: Food and Drug Advisory Committees Conflict of Interest Provisions

The discussion draft requires all individuals under consideration for appointment to serve on an advisory committee to disclose to the Secretary all financial interests that would be affected by the advisory committee's actions. The Secretary would be granted the authority to grant no more than one conflict of interest waiver per committee meeting for an individual if the individual's expertise is necessary for the advisory committee. Disclosure of the waiver would have to be made public 15 or more days prior to the meeting of the advisory committee and would have to be posted on the Internet. The discussion draft spells out a process to allow experts with a financial conflict to present information to the committee. The draft would enhance FDA's outreach activities for identifying non-conflicted experts to participate in advisory committees. Finally, the discussion draft would direct the Secretary to review guidance on conflict of interest waiver determinations with respect to advisory committees at least once every five years and update this guidance as necessary.

Drug Safety: Reagan-Udall Institute for Applied Biomedical Research

The discussion draft would create the Reagan-Udall Institute for Applied Biomedical Research (Institute). The purpose of the Institute is to establish a private-public partnership that would advance FDA's Critical Path Initiative to modernize medical product development, accelerate innovation, and enhance product safety. The draft sets forth the duties of the Institute to include identifying unmet needs in the sciences of developing, manufacturing, and evaluating the safety and effectiveness of diagnostics, devices, biologics, and drugs. Other duties include establishing goals and priorities to meet the identified unmet needs, and awarding grants to advance the goals and priorities identified. The Institute could be funded by appropriations, as well as contributions from the private sector.

Pediatric Devices

The pediatric device discussion draft would offer incentives to device manufactures to create needed medical devices specifically designed to meet the needs of pediatric patients. It would also give FDA the authority to review these devices in a manner distinct from devices in general and to require post-market studies to ensure the continued safety and effectiveness of these devices. The provisions of the discussion draft would only apply to devices that are used in 4,000 or fewer individuals.

The discussion draft would modify the existing humanitarian device exemption (HDE) for medical devices to allow manufacturers of HDE-approved devices specifically designed to meet a pediatric need to make a profit from the sale of such devices. This HDE modification would sunset in 2013. The draft would also authorize FDA to establish a mechanism to track the number and types of devices approved specifically for children or for conditions that occur in children. Finally, the draft discussion would grant explicit authority to FDA's Pediatric Advisory Committee to monitor the use of pediatric devices and to make recommendations for improving their availability and safety.

These discussion drafts will be modified and additional items may be included during their consideration. There is also language in the discussion drafts that states that nothing in these drafts should be construed to modify or otherwise affect any action for damages or the liability of any person for damages under the statutory law or the common law of any State.

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If you have any questions, please contact me or have your staff contact John Ford with the Committee on Energy and Commerce staff at extension 6-2424.